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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,524	02/11/2004	Gosse Jan Adema	DX0670KB1B	8025

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/777,524	ADEMA ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-32* is/are pending in the application.

4a) Of the above claim(s) *30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *21-32* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Appendix A, B

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 21-29, drawn to a substantially pure or isolated polypeptide comprising an amino acid sequence of SEQ ID NO: 2, in the reply filed on 27 April 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 30-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 27 April 2005.

Claims 21-29 are under consideration in the instant application as they read upon SEQ ID NO: 2.

Specification

1. The abstract of the disclosure is objected to because the legal term "said" is used. Applicant is reminded of the proper language and format for an abstract of the disclosure. Correction is required. See MPEP § 608.01(b).

2. The disclosure is objected to because of the following informalities:

2a. The use of the trademarks QIAGEN and GENESCREEN have been noted in this application (See pg 84, line 27; pg 85, line 23). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

2b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "FDF03 POLYPEPTIDE".

Appropriate correction is required.

Claim Objections

3. Claim 21 is objected to because of the following informalities:

3a. Claim 21 recites a non-elected invention (the polypeptide of SEQ ID NO: 4).

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21-29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific, or substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

The claims are directed to a substantially pure or isolated polypeptide comprising an amino acid sequence of SEQ ID NO: 2 or a fragment thereof. The claims also recite an isolated polypeptide comprising residues 1-284 of SEQ ID NO: 2. The claims recite a composition comprising the polypeptide and a polypeptide fused to a detection or purification tag. The claims recite a kit comprising the polypeptide.

The specification discloses that the claimed FDF03 polypeptide comprising the amino acid sequence of SEQ ID NO: 2 is isolated from activated monocytes and is a type I transmembrane protein with an Ig-like extracellular portion (pg 3, lines 3-7). However, the instant specification does not teach any significance or functional characteristics of the FDF03 polynucleotide (SEQ ID NO: 1) or polypeptide (SEQ ID NO: 2). The specification also does not disclose any methods or working examples that indicate the polynucleotide and polypeptide of the instant invention are involved in any activity. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with FDF03. Without any information as to the specific properties of FDF03, the mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed polypeptides. Since significant further research would be required of the skilled artisan to determine how the claimed polynucleotide and polypeptide are involved in any activities, the asserted utilities are not substantial. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. The specification asserts the following as patentable utilities for the claimed putative polypeptide (SEQ ID NO: 2):

1) to produce a variant polypeptide or fusion polypeptide (pg 58, lines 5-37 through pg 64, lines 1-31)

2) to screen for peptides/ligands/drugs which specifically bind/interact with the polypeptide (pg 55, lines 9-37; pg 70, lines 5-16; pg 72, lines 17-37 through pg 74, lines 1-24)

3) to produce antibodies against the polypeptide (pg 50, lines 35-37; pg 54, lines 1-27; pg 57, lines 34-37)

4) to treat conditions associated with abnormal physiology or development; to treat disorders associated with abnormal expression or abnormal signaling by a monocyte (pg 68, lines 22-37 through pg 70, lines 1-4; pg 70, lines 17-37 through pg 72, lines 1-16)

Each of these shall be addressed in turn.

1) to produce a variant polypeptide or fusion polypeptide. This asserted utility is not specific or substantial. Such assays can be performed with any polypeptide. Further, the specification discloses nothing specific or substantial for the variant polypeptide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) to screen for peptides/ligands/drugs which specifically bind/interact with the polypeptide. This asserted utility is not specific or substantial. Such assays can be performed with any polypeptide. Additionally, the specification discloses nothing specific or substantial for the agents that can be identified by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) to produce antibodies against the polypeptide. This asserted utility is not specific or substantial. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, therefore both polypeptide and its

antibodies have no patentable utility. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) to treat conditions associated with abnormal physiology or development; to treat disorders associated with abnormal expression or abnormal signaling by a monocyte. This asserted utility is not specific or substantial. The specification does not disclose which specific disorders or conditions are associated with altered levels or forms of the FDF03 polypeptide. The specification discloses nothing about the normal levels of expression of the polypeptide. Significant further experimentation would be required of the skilled artisan to identify individuals with disorders or conditions are associated with altered levels or forms of the FDF03 polypeptide. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5. Claims 21-29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

However, even if the claimed invention is eventually deemed to have a credible, specific and substantial asserted utility or a well established utility, claims 21 and 23-29 would remain rejected under 35 U.S.C. § 112, first paragraph. The specification of the instant application teaches that the term " polypeptide" includes "a significant fragment or segment of said monocyte protein, and encompasses a stretch of amino acid residues of at least 8 amino acids, generally at least 10 amino acids..." (pg 10, lines 35-37; pg 11, lines 1-2). The specification also

discloses that a mutant monocyte protein encompasses a polypeptide otherwise falling within the homology definition of the monocyte protein, but having an amino acid sequence which differs from that of the monocyte protein as found in nature, whether by way of deletion, substitution, or insertion (pg 60, lines 9-14). However, the specification does not teach any variant, fragment, or derivative of the FDF03 polypeptide other than the full-length amino acid sequence of SEQ ID NO: 2. The specification also does not teach functional or structural characteristics of the polypeptide variants, fragments, and derivatives recited in the claims.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the DNA and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an

active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

6. Claims 21 and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a substantially pure or isolated polypeptide comprising an amino acid sequence of SEQ ID NO: 2 or a fragment thereof. The claims also recite an isolated polypeptide comprising residues 1-284 of SEQ ID NO: 2. The claims recite a composition comprising the polypeptide and a polypeptide fused to a detection or purification tag. The claims recite a kit comprising the polypeptide.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of one FDF03 one polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polypeptides which incorporate all variants and fragments of the polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated polypeptide consisting of the amino acid sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by Torpey et al. (Genbank Accession No. P38928 (previously listed as Accession No. S48394), 02 February 1995).

Torpey et al. teach an isolated polypeptide comprising a fragment of the amino acid sequence of SEQ ID NO: 2 of the instant application (see sequence alignment attached to the Office Action as Appendix A). It is also noted that the Examiner has interpreted the phrase "comprising **an** amino acid sequence of SEQ ID NO: 2" as reading upon fragments of SEQ ID NO: 2, including those only 2 amino acids in length. (It is noted that this rejection could be overcome by amending the claim to recite for example, "A substantially pure or isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 2".)

8. Claims 21, 23-24, and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Chinnadurai, G. (U.S. Patent 5,858,678; application filed 3/21/1995).

Chinnadurai teaches an isolated polypeptide comprising a fragment of the amino acid sequence of SEQ ID NO: 2 of the instant application (see sequence alignment attached to the Office Action as Appendix B; see SEQ ID NO: 31 of Chinnadurai). Chinnadurai also teaches that the polypeptide of SEQ ID NO: 31 is recombinantly produced (col 5, lines 12-13). Chinnadurai discloses that the protein of SEQ ID NO: 31 may be added to culture medium (col 5, lines 40-42, 48-49). As discussed in the 35 USC § 102(b) rejection above, the Examiner has interpreted the phrase "comprising **an** amino acid sequence of SEQ ID NO: 2" as also reading upon fragments of SEQ ID NO: 2, including those only 2 amino acids in length. (It is noted that this rejection could be overcome by amending the claim to recite for example, "A substantially pure or isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 2".)

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Fournier et al. J Immunol 165(3) : 1197-1209, 2000. (FDF03)

Mousseau et al. J Biol Chem 275(6) : 4467-4474, 2000. (PILRalpha; 99.8% sequence similarity to FDF03)

Bates et al. U.S. Patent 6,774,214 (monocyte-derived homolog of FDF03)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
30 June 2005

Bridget E. Bunner
patent examiner